Caboxib

Cabozantinib (S)- malate INN

Composition

Caboxib 20 Capsule: Each capsule contains Cabozantinib (S)- malate INN eqv. to Cabozantinib 20 mg.
Caboxib 80 Capsule: Each capsule contains Cabozantinib (S)- malate INN eqv. to Cabozantinib 80 mg.

Pharmacology

Cabozantinib inhibits the tyrosine kinase activity of RET, MET, VEGFR-1, -2 and -3, KIT, TRKB, FLT-3, AXL, ROS1, TYRO3, MER and TIE-2. These receptor tyrosine kinases are involved in both normal cellular function and pathologic processes such as oncogenesis, metastasis, tumor angiogenesis, drug resistance and maintenance of the tumor microenvironment.

Indications

Cabozantinib is indicated for the treatment of patients with progressive, metastatic medullary thyroid cancer (MTC).

Dose & administration

The recommended daily dose of Cabozantinib is 140 mg once daily without food until disease progression or unacceptable toxicity. Do not eat at least 2 hours before and at least 1 hour after taking Cabozantinib. Swallow Cabozantinib capsules whole. Do not substitute Cabozantinib capsule with Cabozantinib tablets.

Contra-indication

Hypersensitivity to the active substance or to any of the excipients.

Warnings & precautions

Perforations and Fistulas: Monitor for symptoms. Discontinue Cabozantinib for Grade 4 fistula or perforation.
Hemorrhage: Do not administer Cabozantinib if recent history of hemorrhage.
Thrombotic Events: Discontinue Cabozantinib for myocardial infarction or serious arterial or venous thromboembolic events.
Impaired Wound Healing: Withhold Cabozantinib for at least 3 weeks before elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of Cabozantinib after resolution of wound healing complications has not been established.
Hypertension and hypertensive crisis: Monitor blood pressure regularly. Discontinue Cabozantinib for hypertensive crisis or severe hypertension that cannot be controlled with anti-hypertensive therapy.
Osteonecrosis of the Jaw (ONJ): Withhold Cabozantinib for at least 3 weeks prior to invasive dental procedure and for development of ONJ.
Diarrhea: May be severe. Interrupt Cabozantinib immediately until diarrhea resolves or decreases to Grade 1. Recommend standard antidiarrheal treatments.
Palmar-Plantar Erythrodysesthesia (PPE): Interrupt Cabozantinib until PPE resolves or decreases to Grade1.
Proteinuria: Monitor urine protein. Discontinue for nephrotic syndrome. Reversible Posterior Leukoencephalopathy Syndrome (RPLS): Discontinue Cabozantinib.
Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception.

Adverse reactions

The most common adverse reactions (≥ 25%) are diarrhea, stomatitis, palmar-plantar erythrodysesthesia (PPE), decreased weight decreased appetite, nausea, fatigue, oral pain, hair color changes, dysgeusia, hypertension, abdominal pain, and constipation.

Use in Special Population

Pregnancy: Pregnancy Category "D". Based on its mechanism of action, Cabozantinib can cause fatal harm when administered to a pregnant woman.
Lactation: There is no information regarding the presence of Cabozantinib or its metabolites in human milk, or their effects on the breastfed infant, or milk production. Because of the potential for serious adverse reactions in a breastfed infant from Cabozantinib, advise a lactating woman not to breastfeed during treatment with Cabozantinib and for 4 months after the final dose.
Females and Males of Reproductive Potential: Advise females of reproductive potential to use effective contraception during treatment with Cabozantinib and for 4 months after the final dose. Cabozantinib may impair fertility in females and males of reproductive potential.
Pediatric Use: The safety and effectiveness of Cabozantinib in pediatric patients have not been studied.
Geriatric Use: Clinical studies of Cabozantinib did not include sufficient numbers of patients aged 65 years and over to determine whether they respond differently from younger patients.
Hepatic Impairment: Reduce the starting dose of Cabozantinib in patients with mild (Child-Pugh score (C-P) A) or moderate (C-P B) hepatic impairment. Cabozantinib is not recommended for use in patients with severe hepatic impairment.
Renal Impairment: No dose adjustment is recommended for patients with mild or moderate renal impairment. There is no experience with Cabozantinib in patients with severe renal impairment

Drug interaction

Effect of CYP3A4 Inhibitors: Administration of a strong CYP3A4 inhibitor, ketoconazole increased single dose plasma Cabozantinib exposure by 38%. Avoid taking a strong CYP3A4 inhibitor while taking Cabozantinib or reduce the dosage of Cabozantinib if concomitant use with strong CYP3A4 inhibitors cannot be avoided.
Effect of CYP3A4 Inducers: Administration of a strong CYP3A4 inducer, rifampin decreased single-dose plasma Cabozantinib exposure by 77%. Avoid chronic co-administration of strong CYP3A4 inducers with Cabozantinib or increase the dosage of Cabozantinib if concomitant use with strong CYP3A4 inducers cannot be avoided.
Effect of MRP2 Inhibitors: Concomitant administration of MRP2 inhibitors may increase the exposure to Cabozantinib. Monitor patients for increased toxicity when MRP2 inhibitors are co-administered with Cabozantinib.

Overdose

One case of overdosage was reported in a patient who inadvertently took twice the intended dose (200 mg daily) for nine days. The patient suffered Grade 3 memory impairment, Grade 3 mental status changes, Grade 3 cognitive disturbance, Grade 2 weight loss, and Grade 1 increase in BUN. The extent of recovery was not documented.

Storage

Do not store above 25^0 C. Protect from light. Keep out of the reach of children.

Packaging

Caboxib 20 Capsule: Each HDPE container of Caboxib 20 contains 30 capsules, a silica gel desiccant and polyester coil with a child-resistant closure.
Caboxib 80 Capsule: Each HDPE container of Caboxib 80 contains 30 capsules, a silica gel desiccant and polyester coil with a child-resistant closure.

Manufactured by:
ZISKA PHARMA **Ziska Pharmaceuticals Ltd.**
Kaliakoir, Gazipur, Bangladesh
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